Paper No. 25

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BARBRO HEMMENDORFF, ANDREAS CASTAN and ANDERS PERSSON

Appeal No. 2004-0246
Application No. 09/743,023

ON BRIEF

Before WINTERS, MILLS and GREEN, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 1-3, 5-8, and 11-22, which are all of the claims pending in this application.

Claims 1, 2, 5, 8, 12, 15, 18 and 19 are illustrative of the claims on appeal and read as follows:

1. Method for the production of recombinant peptides with a low amount of trisulfides, comprising fermenting cells to produce the recombinant peptides, wherein a metal salt is added during or after the fermentation step, prior to peptide isolation.

2. Method for the reduction of the amount of trisulfides in the production of recombinant peptides comprising fermenting cells to produce the recombinant peptides, wherein a metal salt is added during or after fermentation, prior to peptide isolation.

5. Method according to claim 1, wherein pH is equal to or lower than pH7.

8. Method according to claim 1, wherein the peptide is growth hormone.

12. Method according to claim 1, wherein the peptide is human growth hormone.

15. Method according to claim 2, wherein pH is equal to or lower than pH7.

18. Method according to claim 2, wherein the peptide is growth hormone.

19. Method according to claim 2, wherein the peptide is human growth hormone.

The prior art reference relied upon by the examiner is:

Builder et al. (Builder)	5,663,304	Sept. 1997

Grounds of Rejection

Claims 1-3, 5-8 and 11-22 stand rejected under 35 U.S.C. 102(e), as anticipated by Builder.

The rejections of claims 1, 3, 6-7, 11 and 20; and claims 2, 13, 14,16-17 over Builder are affirmed. The rejection of claims 5, 15 and 22 in view of Builder is vacated. The rejection of claims 8, 12, 18, 19 and 21 under 35 U.S.C. § 102 is reversed.

Claim Grouping

Appellants concede that claims 1, 3, 6-7 and 11[1] (Group 1) stand or fall together and claims 2, 13, 14, 16-17 (Group II) stand or fall together. Brief, page 4. In re Sernaker, 702 F.2d 989, 991, 217 USPQ 1,3, (Fed. Cir. 1983). We decide this appeal

[1] As claim 20 recites related subject matter, we include claim 20 with the subject matter of Group 1. Claim 14 is grouped with the subject matter of Group 2.

on the basis of claim 1 as representative of Group I, and claim 2 as representative of Group II. Appellants further argue claims 5, 8 and 12 are independently patentable from claim 1 and claims 15, 18 and 19 are independently patentable from claim 2. We treat the subject matter of these claims individually in this decision. In Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

DISCUSSION

35 U.S.C. § 102(e)

Claims 1-3, 5-8 and 11-22 stand rejected under 35 U.S.C. 102(e), as anticipated by Builder.

It is the examiner's position that (Answer, pages 3-4):

> Builder et al. teach a method for production of recombinant peptides comprising fermenting cells (host cells) to produce recombinant peptides in the presence of metal salt (alkali metal salt) prior to peptide isolation (see column 26, lines 34-67, column 27, 1-67, column 28, lines 15-33, column 6, lines 42-67, and column 7, lines 1-9). Builder also teach that (i) the use of metals facilitate disulfide oxidation of polypeptides and yield correct refolding of a misfolded polypeptide contained in host cells (see column 6, lines 42-60); metal salts include sodium chloride, potassium chloride, sodium phosphate, potassium phosphate (see column 28, lines 15- 33, column 11, lines 42-54; alkali metal salt buffer (pH 10.5) was added after fermentation and pH was adjusted to 3.5 with phosphoric acid (see column 28, lines 28-33 and column 16, lines 47-55); recombinant polypeptides of interest include human growth factor (see column 8, lines 24-67, and column 9, lines 1-10). Thus the disclosure of Builder et al. meets the limitations in the instant claims.

We agree that the examiner as put forth sufficient evidence to support a prima facie case of anticipation of claim 1. A claim is anticipated only if "each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). In the present case, we agree with the examiner that Builder describes a method comprising fermenting cells to produce recombinant peptides, wherein a metal salt is added during or after the fermentation step, prior to peptide isolation. In particular, Builder describes a fermentation procedure for the production of recombinant insulin growth factor I (IGF-I) in which potassium phosphate (a metal salt) is added during the fermentation procedure, prior to isolation of the peptide. Columns 26 and 27.

Appellants respond, arguing, "While Builder et al disclose that metal salts are provided in the IGF-I fermentation medium, Appellants find no teaching or reference for reducing trisulfide formation in the production of recombinant peptides..." Brief, pages 6-7. Appellants also argue that the preamble of the claim must be given patentable weight. Brief, page 7.

To begin, we find no difference in the manipulative steps between the method recited in claim 1 and that described in the prior art. See In re Sussman, 141 F.2d 267, 270, 60 USPQ 538, 541 (CCPA 1944) ("if appellant obtains a new product through reaction of the elements mentioned, it must be due to some step in the process not included in the claim.")

Moreover, the consideration of preamble claim language is determined on a case by case basis. In the present case, we agree with the examiner (Answer, page 7) that "In the instant invention the limitation 'low amounts of trisulfides' in the preamble of the present claims does not provide any significance to the claim construction because the claims are directed to the production of recombinant polypeptides, but not to the low amounts of trisulfides or formation of reduced trisulfides. Second, even if it is given patentable weight, Builder et al. inherently teaches this limitation by addition metal salt to the process as discussed above."

Moreover, we interpret the claim limitation 'low amount of trisulfides' in the preamble of the claim to include zero or no amount of trisulfides. Compare, In re Mochel, 470 F.2d 638, 639, 176 USPQ 194, 195 (CCPA 1972)("the phrase 'up to' ... includes zero as the lower limit.") and Ex parte Khusid, 174 USPQ 59 (Bd. Pat. App. Int. 1971) ("claims merely recite that the cellulose [has] 'a moisture content of not more than 70 % by weight.' ... since there is no lower limit recited, the claims ... read on dry cellulose, or cellulose containing no more moisture than is normally taken up from the atmosphere. Thus, these claims do not patentably distinguish from the cellulose of the reference which is 'dry in appearance.'")

Here, giving claim 1 its broadest reasonable interpretation consistent with the specification and finding no disclosure of a lower limit on the amount of trisulfides, we conclude that "a low amount of trisulfides" in claim 1 "reads on" no amount; and that the method, as claimed, "reads on" the fermentation method disclosed by Builder.

Appellants also argue that (Brief, page 8):

> [t]he Examiner asserted that the claimed methods are inherently disclosed by Builder et al. as the reference discloses the use of a special buffer to avoid the possibility of producing polypeptides containing disulfide adducts. However, a disulfide adduct, as disclosed in Builder et al, is the product of the interaction between a protein and a reducing agent, such as glutathione, and thus, a disulfide adduct, does not "inherently comprise" trisulfide bonds as the Examiner appears to assert. Further, as acknowledged by the Examiner, Insulin-like Growth Factor (IGF-1) is not known to produce trisulfides when the polypeptide is formed. Thus, Builder et al. cannot inherently teach the present methods of reducing trisulfide amount or formation. Finally, as Builder et al fail to provide a specific teaching in the Examples of the production of a peptide, such as growth hormone, which involves trisulfide formation, the methods presently claimed are not inherent in the teachings of Builder et al.

This argument is without merit. Again, "a low amount of trisulfides" in claim 1 "reads on" no amount; and claim 1 "reads on " the fermentation method disclosed by Builder. The rejection of claim 1 under 35 U.S.C. § 102(e) as anticipated by Builder is affirmed. Claims 3, 6, 7, 11 and 20 fall together with claim 1.

Claim 2

Claim 2 recites the same manipulative steps as claim 1. As discussed above, these steps are described in Builder. There is no difference in the manipulative steps between the claimed method and that of the prior art, and we can find no limitation in claim 2 serving to distinguish the claimed method from that of the prior art. The rejection of claim 2 is affirmed for the reasons set forth with respect to claim 1. As previously indicated, claims 13, 14, 16 and 17 fall together with claim 2.

Claims 5, 15 and 22

Claims 5 and 15 are directed to the methods according to claim 1 or claim 2, respectively, wherein the pH is equal to or lower than pH 7. Claim 22 is a separate independent claim reciting a pH of 7. These claims are ambiguous when read in view of the specification. In particular, Example 1 describes a pH of 7.3 with respect to the cell concentrate, and a pH adjustment of the cell concentrate to 6.5, 7.0 and 7.8. Specification, page 5. The cell concentrates were then adjusted to a pH of 8.2. Additional Examples 2, 3 and 4 describe a pH of 7.2, as well as pHs of 5.9, 6.8, and 7.2 for the cell concentrate at different steps during the fermentation method. Specification, pages 5-6. Thus, claims 5, 15 and 22 would appear unclear as to which cell concentrate solution, at which phase of the process, possesses the claimed pH.

It is well settled that analyzing claims based on "speculation as to meaning of the terms employed and assumptions as to the scope of such claims" is legal error. In re Steele, 305 F.2d 859, 862, 134 USPQ 292, 295 (CCPA 1962). Thus we refrain from speculating as to the meaning of the pH value in claims 5, 15 and 22. We vacate the rejection of claims 5, 15 and 22, and direct the examiner's attention to the "Other Issues" section below.

Claims 8, 12, 18, 19 and 21

Claims 8, 12 depend from claim 1, and claims 18 and 19 depend from claim 2. Claim 21 is a separate independent claim. These claims further characterize the method as one wherein the peptide is growth hormone or human growth hormone.

We find no specific example in Builder teaching a method for producing growth hormone or human growth hormone. While Builder does indicate at column 9, line 18, that a particularly preferred polypeptide which may be produced according to the method of Builder is growth hormone, nevertheless, its selection in combination with a fermenting step as claimed is not clearly and unequivocally disclosed within the meaning of 35 U.S.C. § 102(e). On these facts, such selection does not rise to the level of anticipatory disclosure. The rejection of claims 8, 12, 18, 19 and 21 for anticipation is reversed. We refer the examiner to the "Other Issues" section discussed below, regarding further prosecution of these claims.

Other Issues

Upon return of the application to the examiner, it is recommended that the examiner determine whether a rejection of claims 8, 12, 18, 19 and 21 under 35 U.S.C. § 103 is in order. Although we do not find the disclosure of Builder regarding growth hormone or human growth hormone sufficient to establish a prima facie case of anticipation, the examiner should consider whether a rejection on the statutory basis of obviousness is appropriate in the present case.

In particular, in appropriate circumstances, a single prior art reference can render a claim obvious. See, e.g., B.F. Goodrich Co. v. Aircraft Braking Sys. Corp., 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996); In re O'Farrell, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). However, there must be a showing of a suggestion or motivation to modify the teachings of that reference to the claimed invention in order to support the obviousness conclusion. See B.F. Goodrich , 72 F.3d at 1582, 37 USPQ2d at 1318. This suggestion or motivation may be derived from the prior art reference itself, O'Farrell, 853 F.3d at 902, 7 USPQ2d at 1680, from the knowledge of one of ordinary skill in the art, or from the nature of the problem to be solved. Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1630 (Fed. Cir. 1996); see also Motorola, Inc. v. Interdigital Tech. Corp., 121 F.3d 1461, 1472, 43 USPQ2d 1481, 1489 (Fed. Cir. 1997) (" [T]he suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art."). Determining whether there is a suggestion or motivation to modify a prior art reference is one aspect of determining the scope and content of the prior art, a fact question subsidiary to the ultimate conclusion of obviousness.

In this regard we invite attention to column 9, line 18, of Builder, disclosing that growth hormone is a particularly preferred mammalian polypeptide. The examiner should consider whether it would have been obvious, given the disclosure of Builder, to prepare growth hormone by the fermentation process and recovery procedure at Builder, column 26, wherein metal salt is added during fermentation but prior to peptide

isolation.

Upon return of the application to the examiner, the examiner should consider the applicability of 35 U.S.C. § 112, second paragraph, to claims 5, 15 and 22. Those claims are directed to the method, wherein pH is equal to or lower than pH7. There appears to be some ambiguity present in these claims when read in view of the specification. In particular, Example 1 describes a pH of 7.3 with respect to the cell concentrate, and a pH adjustment of the cell concentrate to 6.5, 7.0 and 7.8. Specification, page 5. The cell concentrates were then adjusted to a pH of 8.2. Additional Examples 2, 3 and 4 describe a pH of 7.2, as well as pHs of 5.9, 6.8, and 7.2, for the cell concentrate. Specification, pages 5-6. Thus claims 5, 15 and 22 would appear unclear as to which cell concentrate solution, at which phase of the process, possesses the claimed pH. The examiner should review the specification and determine the appropriateness of entering a rejection of the claims under 35 U.S.C. § 112, second paragraph.

CONCLUSION

The rejections of claims 1, 3, 6-7, 11 and 20; and claims 2, 13, 14, 16-17 over Builder are affirmed. The rejection of claims 5, 15 and 22 in view of Builder is vacated. The rejection of claims 8, 12, 18, 19 and 21 under 35 U.S.C. § 102 is reversed. The examiner should consider the additional issues raised in the "Other Issues" section of this Decision.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART
REVERSED-IN-PART
VACATED-IN-PART

SHERMAN D. WINTERS
Administrative Patent Judge

DEMETRA J. MILLS
Administrative Patent Judge

LORA M. GREEN
Administrative Patent Judge

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